03-12 02

CPA/1600

BAKER BOTTS L.L.P

CONTINUED PROSECUTION APPLICATION (CPA) REQUEST TRANSMITTAL

Submit an original, and a duplicate for fee processing.

(Only for Continuation or Divisional applications under 37 CFR 1.53(d))

CHECK BOX, if applicable ☐ DUPLICATE

Address to:

Assistant Commissioner for Patents
Box CPA
Washington, DC 20231

Attorney Docket No. of Prior Application	072874.0113
First Named Inventor	Cameron
Examiner Name	Leary. L.
Group Art Unit	1623
Express Mail Label No.	EL740053080US

This is a request for a ☑ continuation or ☐ divisional application under 37 CFR 1.53(d), (continued prosecution application (CPA)) of prior application number 09/444,459, filed on 11/22/99, entitled "Methods and Compositions for Pain * see attached.

NOTES

FILING QUALIFICATIONS: *The prior application identified above must be a nonprovisional application that is either: (1) complete as defined by 37 CFR 1.51(b), or (2) the national stage of an international application in compliance with 35 U.S.C. 371. Effective May 29, 2000, a CPA may only be filed in a utility or a plant application if the prior nonprovisional application was filed before May 29, 2000. A CPA may be filed in a design application regardless of the filing date of the prior application. See "Request for Continued Examination Practice changes to and Provisional Application Practice,"* Final Rule, *65 Fed. Reg. 50092 (Aug. 16, 2000); Interim Rule, 65 Fed. Reg.14865 (Mar. 20, 2000), 1233 Off. Gaz. Pat. Office (Apr. 11, 2000).*

C-I-P NOT PERMITTED: *A continuation-in-part application cannot be filed as a CPA under 37 CFR 1.53(d), but must be filed under 37 CFR 1.53(b).*

EXPRESS ABANDONMENT OF PRIOR APPLICATION: *The filing of this CPA is a request to expressly abandon the prior application as of the filing date of the request for a CPA. 37 CFR 1.53(b) must be used to file a continuation, divisional, or continuation-in-part of an application that is not to be abandoned.*

ACCESS TO PRIOR APPLICATION: *The filing of this CPA will be construed to include a waiver of confidentiality by the applicant under 35 U.S.C. 122 to the extent that any member of the public who is entitled under the provisions of 37 CFR 1.14 to access to, copies of, or information concerning, the prior application may be given similar access to, copies of, or similar information concerning, the other application or applications in the file jacket.*

35 U.S.C. 120 STATEMENT: *In a CPA, no reference to the prior application is needed in the first sentence of the specification and none should be submitted. If a sentence referencing the prior application is submitted, it will not be entered. A request for a CPA is the specific reference required by 35 U.S.C. 120 and to every application assigned the application number identified in such request, 37 CFR 1.78(a).*

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

1. ☐ Enter the unentered amendment previously filed on _____ under 37 CFR 1.116 in the prior nonprovisional application.
2. ☑ An amendment is enclosed.
3. This application is filed by fewer than all the inventors named in the prior application, 37 CFR 1.53(d)(4).
   a. ☐ ***DELETE*** the following inventor(s) named in the prior nonprovisional application:

   b. ☐ The inventor(s) to be deleted are set forth on a separate sheet attached hereto.
4. ☐ A new power of attorney or authorization of agent (PTO/SB/81) is enclosed.
5. Information Disclosure Statement (IDS) is enclosed:
   a. ☐ PTO-1449
   b. ☐ Copies of IDS Citations

03/14/2002 GTEFFERA 00000104 09444459

01 FC:231 370.00 OP
02 FC:203 54.00 OP

BAKER BOTTS L.L.P. Attorney Docket Number: 072874.0113

CLAIMS	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
	TOTAL CLAIMS (37 CFR 1.16(c) or (j))	26 -20* =	6	x $ 18 =	$ 108
	INDEPENDENT CLAIMS (37 CFR 1.16(b) or (i))	3 -3** =	0	x $ 84 =	0
	MULTIPLE DEPENDENT CLAIMS (if applicable) (37 CFR 1.16(d)) ☐			+ $ =	
				BASIC FEE (37 CFR 1.16)	740
				Total of above Calculations =	848
	Reduction by 50% for filing by small entity (Note 37 CFR 1.27).				424
	* Reissue claims in excess of 20 and over original patent. ** Reissue independent claims over original patent.			TOTAL =	424

6. ☑ Small entity status: Applicant claims small entity status. See 37 CFR 1.27.
7. The Commissioner is hereby authorized to credit overpayments or charge any additional fees to Deposit Account No. 02 - 4377 :
   a. ☑ Fees required under 37 CFR 1.16.
   b. ☑ Fees required under 37 CFR 1.17.
   c. ☑ Fees required under 37 CFR 1.18.
8. ☑ A check in the amount of $ 424 is enclosed.
9. ☐ Payment by credit card. Form PTO-2038 is attached.
10. ☐ Applicant requests suspension of action under 37 CFR 1.103(b) for a period of _____ months (not to exceed 3 months) and the fee under 37 CFR 1.17(i) is enclosed.
11. ☐ New Attorney Docket Number, if desired _____
    [Prior application Attorney Docket Number will carryover to this CPA unless a new Attorney Docket Number has been provided herein.]
12. a. ☐ Receipt For Facsimile Transmitted CPA (PTO/SB/29A)
    b. ☐ Return Receipt Postcard (Should be specifically itemized, See MPEP 503)
13. ☑ Other: Petition for Extension of Time under 37C.F.R 1.136(a) and the fee of $200.

NOTE: ***The prior application's correspondence address will carry over to this CPA UNLESS a new correspondence address is provided below.***

14. NEW CORRESPONDENCE ADDRESS

☐ *Customer Number or Bar Code Label* *(Insert Customer No. or Attach bar code label here)* *or* ☐ *New correspondence address below*

Name					
Address					
City		*State*		*Zip Code*	
Country		*Telephone*		*Fax*	

15. SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Name (Print/Type)	Michelle M. LeCointe
Signature	
Registration No. (Attorney/Agent)	46,861
Date	March 11, 2002

BAKER BOTTS LLP

Attorney Docket Number: 072874.0113

Title: "Methods and Compositions for Pain Management"

Use Space Below for Additional Information:

BAKER BOTTS L.L.P.

Attorney Docket Number: 072874.0113

Certificate of Mailing under 37 CFR 1.8

I hereby certify that this correspondence* is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to:

BOX CPA
Assistant Commissioner for Patents
Washington, D.C. 20231

on March 11, 2002
Date

Amy Rueff
Signature

Amy Rueff
Typed or printed name of person of signing Certificate

☑ Express Mail Label No: EL740053080US

* Correspondence

Continued Prosecution Application Request Transmittal
Petition for Extension of Time Under 37 CFR 1.136(a)
Amendment

A31964-072874.0113
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Cameron et al.		
Serial No.	:	09/444,459	Examiner:	Leary, C.
Filed	:	November 22, 1999	Group Art Unit:	1623
For	:	METHODS AND COMPOSITIONS FOR PAIN MANAGEMENT		

AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Official Action dated October 10, 2001, please consider the following amendments and remarks. Applicants request a two month extension of time and enclose the $200 fee as required by 37 C.F.R. 1.17(a)(2). Applicants additionally file a CPA with this amendment. The fee of $370 required under 37 C.F.R. 1.16(a) is also enclosed.

AMENDMENTS

IN THE CLAIMS:

Please cancel Claims 1-20, 26-33 and 55.

Please add Claims 56-81:

56. A method of diagnosing the extent of activation of the pain sensing neurological pathway in a patient comprising:

i) determining the amount of a pain marker in a biological sample obtained from said patient;

ii) comparing the amount of the pain marker in said sample to at least one pre-determined pain marker amount;

iii) assigning a pain status to the patient based upon the comparison.

57. The method of claim 56, wherein the pain marker is cholinesterase.

58. The method of claim 57, wherein the pre-determined cholinesterase amount is a threshold amount determined by:

i) comparing the cholinesterase amount in samples from patients in whom the pain sensing neurological pathway is activated with the cholinesterase amount in samples from normal patients in whom the pain sensing neurological pathway is not activated; and

ii) setting the threshold so that the average or mean cholinesterase amount in samples from normal individuals is below the threshold amount while the average or mean cholinesterase amount in samples from individuals in whom the pain sensing neurological pathway is activated is above the threshold amount.

59. The method of claim 58, wherein the threshold is set at least three standard deviations above the mean cholinesterase amount in samples from normal individuals.

60. The method of claim 58, wherein additional cholinesterase amounts are set as indicative of increasing levels of pain sensing neurological pathway activation by comparing the mean or average cholinesterase amounts of individuals with higher levels of pain sensing neurological

pathway activation with mean or average cholinesterase amounts of lower levels of pain sensing neurological pathway activation and selecting an amount between the two means or averages.

61. The method of claim 56, wherein the pain sensing neurological pathway is activated by chronic spinal pain.

62. The method of claim 61, wherein the sample is blood or serum and the cholinesterase is serum cholinesterase.

63. The method of claim 62, wherein the pre-determined serum cholinesterase threshold amount is 1272 and patients from whom the sample contains less than this amount of serum cholinesterase are deemed to have normal activation levels of the pain sensing neurological pathway while patients from whom the sample contains greater than this amount of serum cholinesterase are deemed to have high or activated activation levels of the pain sensing neurological pathway.

64. The method of claim 56 further including the step of separating components within the biological sample.

65. The method of claim 64 wherein separating comprises an electrophoretic separation.

66. The method of claim 57, wherein the cholinesterase in the biological sample is reacted with a substrate to produce a detectable product.

67. The method of claim 57, wherein the pre-determined cholinesterase amount is based upon at least one biological sample of the same type from the same patient obtained prior to the diagnosis of activation of the pain sensing neurological pathway.

68. The method of claim 67, wherein the prior obtained biological sample was obtained at a time when the patient's pain sensing neurological pathway was unactivated or at a normal activation level and the patient is deemed to have an activated or high level of pain sensing neurological pathway activation if the diagnosis sample contains a statistically significant greater amount of cholinesterase than the prior obtained sample.

69. The method of claim 56 , wherein the activation of the pain sensing neurological pathway is caused by the presence of a lesion.

70. The method of claim 57, whereby cholinesterase may be distinguished and measured by

eserine sensitivity.

71. A method for determining the efficacy of a treatment for pain comprising:

i) determining the amount of a pain marker in a first biological sample obtained from said patient;

ii) administering the treatment to said patient;

iii) determining the amount of a pain marker in a second biological sample obtained from said treated patient; and

iv) comparing the amount of the pain marker in the first and second biological samples.

72. The method of claim 71, in which the pain marker is cholinesterase.

73. The method of claim 72, wherein a statistically significant decrease in the amount of cholinesterase in the second sample is indicative of treatment efficacy while an increase or no

statistically significant change in the amount of cholinesterase in the second sample is indicative of treatment inefficacy.

74. The method of claim 71, wherein the treatment is an analgesic compound.

75. The method of claim 74, wherein the analgesic compound comprises aspirin, acetopinophen, codeine, morphine, butorphanol, diperone, fenoprofen, fentanyl, banamine or combinations thereof.

76. A diagnostic kit for determining the level of activation of the pain sensing neurological pathway in a patient comprising at least one agent that reacts with cholinesterase in a biological sample obtained from a patient wherein the amount of cholinesterase in the sample is then compared with an amount of cholinesterase known to be indicative of activation of the pain sensing neurological pathway.

77. The diagnostic kit of claim 77, wherein the agent comprises at least one antibody which binds with cholinesterase.

78. The diagnostic kit of claim 77, wherein the antibody or antibodies are polyclonal

antibodies, monoclonal antibodies or fragments of polyclonal or monoclonal antibodies.

79. The diagnostic kit of claim 76, wherein the agent is a substrate for cholinesterase.

80. The diagnostic kit of claim 79, wherein the substrate is acetylcholine, an acetylcholine analog, 4-chloro-methylaniline or any combination thereof.

81. The method of claim 76 wherein cholinesterase is distinguished and measured based upon eserine sensitivity.

REMARKS

This Response is filed to the Office Action dated October 10th, 2001. The Examiner has rejected claims 1-20, 26-29 and 32, 33 and 55 under 35 U.S.C. §102(b) as being anticipated or, alternatively, under 35 U.S.C. § 103(a) as being obvious in light of US Patent 3,928,594 (Cook). The Examiner has objected to claims 30 and 31 as being dependent upon a rejected base claim, in this case claim 29, but has indicated that these claims would be allowable if rewritten in independent form. Claims 21-25 were deemed allowable over the prior art record. Applicants have cancelled Claims 1-20, 26-33 and 55 and have added new Claims 56-81.

Applicants thank the Examiner for her telephone interview on January 16, 2002 concerning this application. During the interview, the Examiner clarified that she believes that Applicants' recitation of determining the amount of a biological marker in, *inter alia*, Claim 1, is equivalent to determining the activity in the case of an enzyme. Further, the Examiner explained that Cook discloses a determination of the activity of cholinesterase. The Examiner additionally clarified that she believes Cook discloses that cholinesterase is a biological marker which "correlates" with pain within the bounds of, *inter alia*, Claim 1 because the reference indicates that, in demyelination disorders in which cholinesterase activity is modified, a symptom of the disorder is pain.

Applicants note that no version of the claims marked to show changes made is required because all claims pending after amendment are new.

Rejections

All rejected claims have been cancelled, rendering the rejections moot.

Comments on New Claims

In order to facilitate examination of this application, Applicants provide the following commentary on the new claims, explaining how certain issues raised in relation to the cancelled claims do not apply to these new claims.

First, Applicants note that Claim 69 recites pain caused by the presence of a lesion. This is supported in the Specification, *inter alia*, at Page 28, Lines 20-22.

Second, Applicants note that a great deal of confusion seems to have resulted from the alleged lack of more specific steps in Applicants' previous method claims and more specific components of Applicants' kit claims. Although Applicants believe that, for instance, the "method" of Claim 1 is properly read in light of the specification to include a variety of details not present in Cook, in order to advance prosecution Applicants have provided new claims which explicitly include these steps. Applicants note that because these steps were previously inherent in the cancelled claims, the cancellation of old claims and presentation of new claims in no way narrows the claimed subject matter.

Support for Applicants' addition of these steps may be found throughout the specification, especially in the Examples such as on Page 29, Lines 9-11.

Applicants' new claims are clearly distinguishable from Cook, which provides no steps for diagnosing pain based on cholinesterase amount.

Allowable Claims

Applicants note that the Examiner has indicated that Claims 21-25 are allowable. Applicants have neither amended nor cancelled these claims and thank the Examiner for her consistent recognition of their allowability.

CONCLUSION

Based on the foregoing remarks, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is therefore respectfully requested.

Applicants believe a fee in the amount of $200 is required for a two month extension of time under 37 C.F.R. 1.17(a)(1) and a fee in the amount of $424 is due for a CPA, accordingly, checks in the amounts of $200 and $424 are enclosed. Applicants believe no

additional fees are due. Should any additional fees be due for this or any other communication, the Commissioner is hereby authorized to charge Deposit Account Number 02-4377. Two copies of this page are enclosed.

Respectfully submitted,

BAKER BOTTS, L.L.P.

By: _____

Rochelle K. Seide
Patent Office Reg. No. 32,300
Attorney for Applicants

Michelle M. LeCointe
Patent Office Reg. No. 46,861
Attorney for Applicants

30 Rockefeller Plaza
New York, NY 10112

(512) 322-2580